

REMARKS

Following entry of the foregoing amendments, claims 1-19, 34-38, and 40-45 constitute the pending claims in the present application. Claims 20-33 and 39 are cancelled. Claims 40-45 are newly added.

Telephonic Interview with Examiner

Applicants greatly appreciate Examiner Maier's time and attention during the numerous telephonic interviews during the first half of April 2007. During the telephonic interviews, the pending claims were discussed, and it was agreed that the present amendments will place the application in condition for allowance.

Amendments and New Claims

Applicants note that per the Advisory Action of March 16, 2007 the amendments made in Applicants' first Reply (mailed February 13, 2007) to the outstanding Final Office Action were not been entered. Accordingly, the present amendments are made to the claims as they stood following entry of Applicants' Reply mailed July 18, 2006.

As indicated in more detail below, Applicants have amended claims 1 and 3-4 to more particularly claim the present invention and as discussed with the Examiner. Applicants have also amended claims 2 and 4 for clarity and claims 5-6 and 10 to correct antecedence.

Applicants have added new claims 40-43. Support for these claims can be found in the specification as originally filed, for example, on page 1, lines 21-22; page 3, lines 10-11; page 17, lines 16-17; page 37, lines 25-27; and pages 76-80. Applicants have also added new claims 44-45, which recite subject matter from claim 1 as unamended. During the telephonic discussions, the Examiner indicated that these claims would be allowable.

In order to expedite prosecution, Applicants have cancelled claims 21-26 and 28-33, which were formerly withdrawn. The Examiner indicated that cancellation of these claims was required to put the application in condition for allowance. Applicants have also cancelled claim 39 to advance prosecution.

The present amendments and new claims present no new matter. Applicants reserve the right to pursue any of cancelled claims 20-33 or any of the present claims in their unamended form in one or more divisional and/or continuation applications.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

I. Claim Rejections – 35 U.S.C. 112, Second Paragraph

Claims 1-19 and 35-39 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for allegedly failing to point out and distinctly claim the subject matter which Applicants regard as the claimed invention. The Office contends that it is not clear how the previous amendments reciting “linear” polymers differ from “branched” polymers since “the structural formulas appear to allow for a structure that is consistent with the specification’s description of ‘branched.’”

Applicants disagree and respectively highlight that the specification at paragraph 0082 of the published application states that “a branched cyclodextrin-containing polymer refers to a polymer *backbone* with a plurality of branch points, wherein each branch point is a starting point of yet *another* strand of the polymer *backbone*.¹” (emphasis added). Applicants further submit that “backbone” is an art-recognized term that refers to the polymer chain(s) that includes the repeating chemical units of the polymer. Thus, a “branched” polymer is distinct from a “linear” polymer, which the art recognizes as a polymer with a backbone including no additional branching. Applicants respectfully point out that polymers which include pendant side chains emanating from a linear backbone fall within the ambit of “linear” polymers, provided of course that the side chains are not additional backbones, *i.e.*, that the side chains do not comprise repeating chemical units of the linear backbone. Hence, the present claims are directed to polymers with linear backbones and thus exclude polymers with branched backbones. The present claims either recite the linear feature in words (claims 1, 3, 4, and 34) or explicitly in the formulas (claims 2, 3, and 4 depict the polymer backbone as having only two points of attachment extending from the monomer, thus depicting a linear polymer) and convey with clarity and definiteness the claimed subject matter. Accordingly,

Applicants request reconsideration and withdrawal of the indefiniteness rejection over claims 1-19 and 35-38. As claim 39 has been cancelled, the rejection is rendered moot for this claim.

Additionally, the Office considers claim 1 to be unclear, in particular the antecedence for “linker.” Since the present amendments delete recitation of “linker moieties” from claim 1, Applicants assert that any lack of clarity resulting in the recitation of “linker moieties” has been corrected and that claim 1 is clear and definite.

2. *Claim Rejections – 35 U.S.C. 112, First Paragraph*

Claims 1, 2, 5-19 and 35-38 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that Applicants had possession of the claimed invention at the time of filing. Specifically, the Office submits that page 16, lines 1-4 of the specification as originally filed does not support the feature of claim 1 “wherein at least one linker moiety includes a therapeutic agent.”

Although Applicants disagree, to expedite prosecution, Applicants have deleted the objected phrase from claim 1. Applicants have in turn amended the objected phrase to recite “wherein a plurality of linker moieties ...” and included this subject matter in new claim 45. The Office has indicated that language utilizing the term “plurality” is supported. Moreover, Applicants submit that the skilled artisan, on reading page 16, lines 1-4 of the specification as originally filed, to say nothing of the many examples described, would conclude that the specification teaches a polymer having a plurality of linker moieties attached to therapeutic agents. As such, Applicants request reconsideration and withdrawal of the written description rejection over claims 1, 2, 5-19 and 35-38.

3. *Claim Rejections – 35 U.S.C. 102(b) over WO 00/01734 to Gonzalez et al.*

Claims 1-3, 5, 7, 10-18, 35, and 38-39 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by WO 00/01734 to Gonzalez et al. (“Gonzalez”). Applicants traverse the rejection to the extent that it is maintained over the claims as amended.

As noted previously, according to the Office, Gonzalez discloses linear cyclodextrin copolymers including an embodiment wherein a folic acid moiety is covalently attached to a copolymer. The Office considers that “ligands” in the art and “therapeutic agents” of the claims are not mutually exclusive. The Office further considers that the folic acid moiety is described in Gonzalez as a ligand “similar to the ‘targeting ligands’ in the instant invention” and that the folic acid moiety “is also consistent with Applicant’s definition of therapeutic agent.”

Nevertheless, Applicants assert that Gonzalez does not teach or suggest all the features of claims 1 and 3 as currently amended. In particular, regarding claim 1, Gonzalez does not teach or suggest a polymeric compound comprising therapeutic agents attached to the polymer chain through attachments that are cleaved under biological conditions. Without conceding that folic acid is a therapeutic agent, Applicants note that folic acid in the embodiments of Gonzalez is not taught or suggested to be releasable.

Regarding claim 3, Applicants again note that Gonzalez does not teach or suggest linear polymeric compounds with the particular structure of Formula II recited therein, *i.e.*, polymers with one or more cyclodextrin moieties or derivatives *not* part of the polymer chain/backbone. The Office appears to consider that claim 3 requires a cyclodextrin and a therapeutic agent be present *anywhere*. Applicants respectfully disagree and point out that in the language of claim 3 “CD” is not interchangeable with “cyclodextrin” (otherwise the claim would be inconsistent in using both of these terms). Rather, as recited in the claim, CD represents a cyclodextrin moiety or derivative thereof *at the specified position* as recited in Formula II, *i.e.*, at a position on a pendant side-chain. Claim 3 recites that CD (not simply a cyclodextrin) is present at least once in the compound. Thus, for at least one occurrence of “n,” “n” is not equal to 0. Applicants further highlight that there can be many occurrences of “n,” since there can be as many as 30,000 repeating units of Formula II, and that the occurrences of “n” are *independent*. Consequently, the compound of claim 3 recites that there is at least one cyclodextrin moiety or derivative thereof that is not part of the polymer chain/backbone but positioned on a side chain (*i.e.*, at least one CD). This is a feature that is not taught or suggested in Gonzalez.

Since claim 39 has been cancelled, the rejection is rendered moot for this claim.

Since a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference (see MPEP 2131, quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)), Gonzalez does not anticipate claim 1 or 3 or any claims dependent thereon. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

4. Claim Rejections – 35 U.S.C. 102(b) over Hristova-Kazmierski, Minami, Yano, and Tanaka

Claims 3-5, 7, 10-16, 19, and 35 remain rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Hristova-Kazmierski et al. *Bio. Med. Chem. Lett.* **1993**, 3, 831-834 (“Hristova”); Minami et al. *J. Pharm. Sci.* **1998**, 87, 715-720 (“Minami”); Yano et al. *J. Pharm. Sci.* **2001**, 90, 493-503 (“Yano”); or US 5,183,883 to Tanaka et al. (“Tanaka”). Applicants traverse the rejection to the extent that it is maintained over the claims as amended.

Applicants previously argued that Hristova, Minami, Yano, and Tanaka do not teach or suggest all the limitations of claims 3-4. Notably, these references do not teach or suggest linear *polymeric* compounds such as those depicted in Formulas II and III of claims 3 and 4, respectively. In response to Applicants’ arguments of record, the Office has not given patentable weight to the term “polymeric.” Accordingly, to advance prosecution, Applicants have further specified the presently claimed compounds by amending integer variables “o” in claim 3 and “h” in claim 4 to represent an integer in the range of 2 to about 30,000. As Hristova, Minami, Yano, and Tanaka provide monomeric compounds, these references do not teach or suggest the presently claimed compounds and cannot be said to anticipate claims 3 or 4 or claims dependent thereon. Applicants request reconsideration and withdrawal of the rejection.

5. Claim Rejections – 35 U.S.C. 103(a) over WO 00/01734 to Gonzalez et al.

Claims 1-3, 5, 7, 12-19, and 35-39 stand rejected under 35 U.S.C. 103(a) as allegedly being obvious in view of Gonzalez. Applicants traverse the rejection to the extent that it is maintained over the claims as amended.

The Office acknowledges that Gonzalez does not exemplify “a polymeric compound comprising cyclodextrin moieties alternating with linker moieties in the polymer chain ... wherein at least one linker moiety includes a therapeutic agent.” Nevertheless, the Office alleges that Gonzalez does in fact suggest such a product, referring to the paragraph bridging pages 13 and 14 of Gonzalez. Applicants still do not concede that “ligands” recited in Gonzalez include “therapeutic agents” as recited in the present claims. Moreover, regarding claim 1, Applicants further highlight that Gonzalez does not recite that the ligands recited therein are cleaved under biological conditions as recited for the therapeutic agents in the final line of claim 1. Hence, as noted above, Gonzalez does not teach or suggest all the claimed features of claim 1. Concerning claim 3, again Gonzalez does not teach all the features of this claim, in particular, polymers with one or more cyclodextrin moieties or derivatives *not* part of the polymer chain/backbone. Since claim 39 has been cancelled, the rejection is rendered moot for this claim.

Consequently, Gonzalez does not teach or suggest all the features of claims 1 or 3 or those dependent thereon. Pursuant to MPEP 2142, “[t]o establish a prima facie case of obviousness...the prior art reference (or references when combined) must teach or suggest all the claim limitations.” *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). As such, the present claims are non-obvious over Gonzalez, and Applicants respectfully request reconsideration and withdrawal of the rejection.

6. Claim Rejections – Obviousness-Type Double Patenting over US 6,884,789 and US 6,509,323

Claims 1-3, 5, 7, 12-19, and 35 stand rejected under the judicially created doctrine of obviousness-type double patenting over claim 7 of US 6,884,789 (“the ‘789 patent”) and over claim 4 of US 6,509,323 (“the ‘323 patent”). Applicants traverse the rejection to the extent that it is maintained over the claims as amended.

The Office maintains the above rejection continuing to rely on the *specifications* of the ‘789 and ‘323 patents to read into the claims of these patents limitations that are simply not there. In particular, the Office alleges that claims 3 and 8 (apparently of the ‘789 and ‘323 patents,

respectively) recite the use of linkers comprising functional groups “suitable for attaching a ligand, as suggested in the *written description* of the products...” (emphasis added). Although the specification of the patent supporting the rejection may be relied on to interpret terms in the claims of the patent, as Applicants have noted previously, reliance on the written description of the cited art to import features not recited in the claims is improper in the context of an obviousness-type double patenting rejection (MPEP 804). Hence, the present obviousness-type double patenting rejections should be withdrawn for at least this reason.

Moreover, the Office still has advanced no rationale or evidence to satisfy the obviousness requirements of motivation and reasonable expectation of success of the outstanding obviousness-type double patenting rejection. For the requirement that the cited art must teach all the limitations of the present claims, Applicants note that neither claim 7 or 3 of the ‘789 or ‘323 patent, respectively, teaches or suggests a polymer comprising “cyclodextrin moieties ... wherein a plurality therapeutic agents or prodrugs thereof are covalently attached to the polymer chain through attachments that are cleaved *under biological conditions*” as recited in present claim 1. (emphasis added). Similarly, for claim 3, the Office has not indicated where claim 7 or 3 of the ‘789 or ‘323 patent, respectively, teaches or suggests the particular features of the polymer claimed, such as polymers with one or more cyclodextrin moieties or derivatives *not* part of the polymer chain/backbone.

In light of the deficiencies mentioned above of the present obviousness-type double patenting rejection, Applicants request reconsideration and withdrawal of the rejection of claims 1 and 3 and claims dependent thereon.

7. Allowable Subject Matter

Applicants appreciate the indication of allowance of claim 34. Applicants assert that the amendments made herein do not in anyway affect the Office’s determination that claim 34 is allowable.

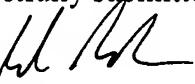
CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited.

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to Deposit Account No. 18-1945, under Order No. ITI-P01-008, from which the undersigned is authorized to draw.

Dated: April 17, 2007

Respectfully submitted,

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